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CASE REPORT

Epidermal Cysts in a Tacrolimus Treated Renal Transplant Recipient

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Tacrolimus, a calcineurin inhibitor, formerly also known as FK506, is a macrolactam drug isolated from *Streptomyces tsukubaensis*. Its mode of action closely parallels the action of cyclosprorin A (CsA) and can be used for the treatment of inflammatory and autoimmune skin diseases in which systemic CsA has proved effective against psoriasis, pyoderma gangrenosum, atopic dermatitis, lupus erythematosus and graft versus host disease (GVHD). Although several cases of epidermal cysts have been reported in patients using cyclosporine and other immunosuppressants after organ transplantation; such types of cases have yet not been reported after administration of tacrolimus. However, we report herein a case of presence of multiple, various sized epidermal cysts in a renal transplant recipient receiving tacrolimus. **(Ann Dermatol 23(S2) S182～S184, 2011)**

-Keywords-
Epidermal cyst, FK506, Immunosuppressant, Renal transplant, Tacrolimus

INTRODUCTION

Epidermal cyst is a keratin-filled lesion lined by epidermis. It is found most commonly in both male and female adults and is presented as single or multiple, intradermal or subcutaneous masses[1]. This cyst is most commonly the result of plugged pilosebaceous units and can also be caused by the traumatic implantation of epidermal cells or by the proliferation of variable epidermal remnants[2]. Recently, human papillomavirus (HPV) type 57 and 60 DNAs have been regarded as etiological factors[1,2]. Immunomodulatory drugs, such as cyclosporine or tacrolimus are mainly used as immunosuppressants in organ transplantation recipients. They have recently been in the spotlight as treatment options for psoriasis, atopic dermatitis, alopecia areata and other dermatologic diseases. Tacrolimus, formerly known as FK506, is a macrolactam drug isolated from *Streptomyces tsukubaensis*[1]. Although tacrolimus has no structural homology to cyclosporine A (CsA), its mode of action closely parallels CsA, and it exerts similar *in vitro* effects at concentrations of 100 times lower than those of CsA[3]. Tacrolimus affects numerous aspects of cellular physiology, mainly alteration of gene expression in target cells. In particular, interleukin-(IL) 2 gene expression in CD4+ T-helper lymphocytes is inhibited by tacrolimus[4]. Although several cases of epidermal cysts have been reported in patients using cyclosporine and other immunosuppressants after organ transplantation, such types of cases have yet not been reported after administration of tacrolimus[2,3,5]. We report a case of presence of multiple, various sized epidermal cysts

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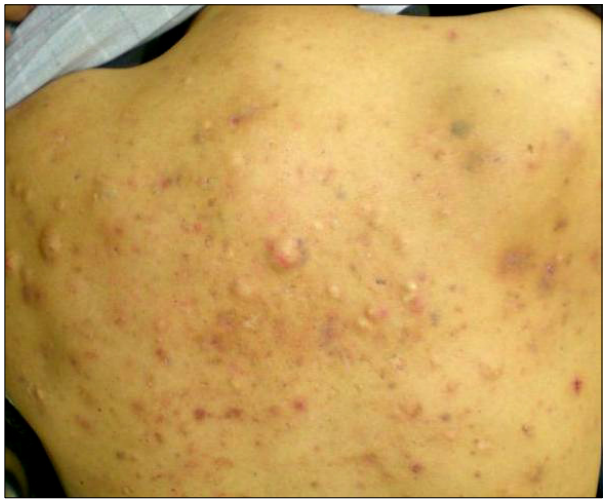

Fig. 1. Multiple scattered 0.5～3 cm sized nodules and tumors on the back.

in a renal transplant recipient receiving tacrolimus.

CASE REPORT

A 44-year-old male patient was presented with a 1 year history of presence of multiple (>100) cystic masses of varying sizes on his neck, back and buttocks. There was no definite family history of presence of multiple masses on the skin. Oral tacrolimus was administered at an initial dose of 10 mg/day and was decreased to a maintenance dose of 4 mg/day during the first 6 months of transplantation. Oral steroid (an initial dose of 60 mg/day) was tapered and discontinued after 3 months of transplantation. No steroids were administered over the past 4 years. After 3 years of operation, more than 100 nodules and tumors (0.5～3 cm diameter) occurred on his back and neck. They increased in size and number, and some of the cysts were infected (Fig. 1). After an excisional biopsy, there were neither new lesions nor changes in previous skin lesions, such as partial response or progression. In the meantime, the patient continued to take a low oral dose of tacrolimus (4 mg/day).

DISCUSSION

The frequency of organ transplantation has been rapidly increasing in recent years. Accordingly, the use of immunosuppressants has risen dramatically. There are several kinds of immunosuppressants: calcineurin inhibitors (cyclosporine, tacrolimus and pimecrolimus) in the macrolactam group and rapamycin inhibitors (sirolimus and everolimus). Above all, cyclosporine and tacrolimus are widely utilized because of their effect on humoral and cellular immunity, especially when they come in contact with T-helper cells during the early phase[3]. A previous study reported that epidermal cyst occurred in 28% of 67 patients receiving cyclosporine after renal transplantation. Koranda et al.[6] reported that no epidermal cyst was found in 200 patients undergoing renal transplantation who were not administered cyclosporine. Tacrolimus is in the same group as cyclosporine and is structurally different from cyclosporine, but has a similar mechanism of action. As per the literature survey, there have been few reports on occurrence of epidermal cysts after administration of tacrolimus. Some of the investigators have demonstrated that cyclosporine promotes keratinization, resulting in hair follicle occlusion and causing epidermoid cysts[2]. We can postulate that tacrolimus might elicit a similar reaction as cyclosporine. It has been indicated that dendritic epidermal T cells secrete keratinocyte growth factor; thereby promoting the proliferation of keratinocytes[7]. Tacrolimus may affect T cells by influencing the manifestation of keratinocytes so that they can act on the occurrence of mucocutaneous diseases, such as epidermal cysts. It is unclear whether HPV is truly an etiological factor or just a chance association. Recently, HPV type 57 and 60 DNAs have been detected in palmoplantar epidermal cysts. It is considered that tacrolimus induced immune suppression may influence HPV infection. Lee et al.[8] have shown that HPV can be detected in nonpalmoplantar skin lesions. In our case, it seems likely that HPV infection may be associated with the skin lesions although HPV immunostain was not detected. Steroid-induced acneiform eruption may be attributed to administration of a high dose of steroid. However, the clinical and histological findings established a diagnosis of multiple epidermal cysts rather than acneiform eruption. Our patient received a high dose of tacrolimus 3 years ago, which was then gradually decreased. Thereafter, the patient continued to take it at a maintenance dose. In our case, the epidermal cyst seemed to occur due to a low dose of tacrolimus. Although epidermal cysts related to cyclosporine usually occur within 3 or 4 months of the initial treatment, in our case, the cysts occurred at an unusually late rate[2,3]. This may be due to the characteristics of tacrolimus, which shows fewer side effects at a relatively low concentration[4,9]. Tacrolimus has received much attention not only in terms of post-transplantation immune suppression, but also in dermatologic treatment, exhibiting outstanding efficacy. In our report, we have presented a very rare side effect of tacrolimus.

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